Remarks

Claims 7 and 13-20 are pending and were rejected in the Office Action mailed May 19, 2004.

Applicants appreciate the telephonic interview with Examiner Schultz on June 15, 2004, wherein claim rejections under 35 U.S.C. 112 were discussed, and wherein the cited prior art was contrasted to the present invention.

Applicants have herewith amended claims 7, 13, and 17-19.

Rejection of claims 7 and 13-16 under 35 USC 112 second paragraph

The Examiner has rejected claims 7 and by dependency claims 13-16 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and claim the subject matter of the invention. The Examiner has pointed out that there is no antecedent basis for the phrase "the aminoacylated ribozyme" in the claims. Applicants have amended claim 7 in accordance with the Examiner's suggestion for providing proper antecedent basis and respectfully request removal of the stated rejection.

Rejection of claims 17 and 18-20 under 35 USC 112 second paragraph

The Examiner has rejected claims 17 and by dependency claims 18-20 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and claim the subject matter of the invention.

The Examiner argues that claim 17 recites a method for constructing cis-aminoacylating catalytic RNA molecules, but the method steps indicate that such molecules are already constructed because the method steps test whether any of the already-constructed molecules have the inherent ability to become cis-aminoacylated. In response, Applicants have amended claim 17 to be directed to a method of identifying cis-aminoacylating catalytic RNA molecules, rather than constructing such molecules, and respectfully request removal of the stated rejection.

Rejection of claims 17, 14-17, 19 and 20 under 35 USC 112 first paragraph

The Examiner has rejected claims 7, 14-17, 19 and 20 under 35 USC 112, first paragraph, as failing to comply with the written description requirement with respect to the phrase "tRNA-like".

In response, Applicants have amended the claims to replace "tRNA-like" with "tRNA". Applicants point out that the meaning of "tRNA" is well known to those skilled in the art and therefore request the Examiner to remove the state rejection.

Rejection of claims 7 and 17 under 35 USC 102

The Examiner has rejected claims 7 and 17 under 35 USC 102(b) as being anticipated by Lohse et al. (Nature, 1996. 381:442-4). The Examiner argues Lohse et al. describes constructing a pool of RNA molecules, each containing a ribozyme along with both random and constant domains. The Examiner asserts that Lohse et al. further describes introducing a 3' fragment of a charged tRNA molecule to the pool and then enriching the fragment of the constructed RNA molecules that undergo cis-aminoacylation via utilization of the tRNA fragment as an amino acid donor. The Examiner argues Lohse et al. therefore anticipates the instant claims because the term "tRNA-like" is considered to be sufficiently broad that the disclosure meets the claim limitations of the present application.

In response, Applicants point out that the present claims have been amended to replace "tRNA-like" with "tRNA". Applicants further point out that the disclosure of Lohse et al. results in the transfer of an amino acid from the 3' end of an RNA heptanucleotide to the 5' end of a ribozyme (see Figure 1, p 442), and the method of the present invention is therefore distinct from Lohse et al., as follows:

In Lohse et al., the amino acid substrate is provided at the outset of the reaction as an RNA heptanucleotide that is aminoacylated at its 3' end. The method described in Lohse et al. results in the identification of a ribozyme that can aminoacylate its own 5' end by using the aminoacylated RNA heptanucleotide as an amino acid donor. This substrate is intended to mimic an amino acid conjugated to a hydroxyl group for the purpose of investigating the peptidyl transfer reaction that takes place on the ribosome. (See the Abstract, p 442 of Lohse et al.).

In contrast, the present invention utilizes an amino acid substrate that is not conjugated to RNA at the outset of the reaction. Further, the method of the present invention identifies molecules that can catalyze transfer of an amino acid to the 3' end of a tRNA domain, rather than the 5' end of a ribozyme as disclosed in Lohse et al. Support for the aminoacylation event occurring at the 3' end of the tRNA domain in the present invention is provided by the fact that the 5' end of the tRNA domain is bound in a phosphodiester linkage with the 3' end of the ribozyme. Therefore, the 5' end of the tRNA domain is not accessible for aminoacylation in the present invention. Additional data demonstrating the 3' end of the tRNA domain is the aminoacylation site is presented on page 15, lines 35-37, and page 16, lines 1-2 of the present application.

Applicants have amended claims 7 and 17 to emphasize this distinction and therefore respectfully submit that Lohse et al. does not anticipate the present invention. Lohse et al. does not anticipate the present invention because the method disclosed therein cannot be used to identify molecules that can aminoacylate their own 3' ends. Rather, the disclosure of Lohse et al. provides a method for identifying a ribozyme that can aminoacylate its own 5' end, and in particular provides no teaching whatsoever as to how to identify a molecule that can aminoacylate a tRNA domain at its own 3' end.

Applicants further point out an additional distinction between the method of Lohse et al. and the present invention. Lohse et al. requires the inclusion of an RNA component of the amino acid substrate as a critical feature of the method disclosed therein. For example, in the legend to Figure 3 on page 443, and near the bottom of the first column of page 442, the authors note that the most striking feature of the ribozymes they identified is a 100% conserved sequence at the 5' end of the ribozyme which is complementary to the RNA heptanucleotide component of the amino acid substrate. On page 442, in the first paragraph of column 2, the authors indicate that this complementarity is understood to bring together the aminoacyl group of the substrate and the 5' end of the pool RNA.

The importance of this complementarity is emphasized on page 444, left column, first full paragraph, where the authors point out that no acyl transferase activity was observed unless the terminal phosphates were removed from the 5' end of the ribozyme. This result is interpreted

therein as meaning the free 5' end of the ribozyme can act as a nucleophile when it is in proximity to the aminoacyl group of the substrate. Such proximity is believed to be due to the complementarity between the RNA component of the substrate and the ribozyme as explained on page 444, left column, first full paragraph.

In contrast, the present invention provides self-aminoacylating molecules that do not require nucleotide complementarity with the amino acid substrate and can further aminoaclyate their own 3' ends with an amino acid substrate free from a ribo-oligonucleotide conjugate. Applicants have amended claims 7 and 17 to reflect this distinction.

The Examiner also rejected claims 7 and 17 under 35 USC 102(b) as being anticipated by Suga et al. (J.Am.Chem.Soc. 1998. 120:1151-1156). However, the Suga et al. reference is an elaboration of the structural and kinetic characteristics of the ribozyme and reaction disclosed in the Lohse et al. reference described above. Applicants also point out that the Suga et al. reference further emphasizes the importance of the interaction between the RNA component of the amino acid substrate and the ribozyme to facilitate aminoacylation of the 5' end of the ribozyme (for example, on page 1151, second column). In contrast, Applicants point out that the present invention provides self-aminoacylating molecules that do not require nucleotide complementarity with the amino acid substrate and can further aminoaclyate their own 3' ends with an amino acid substrate free from a ribo-oligonucleotide conjugate, and Applicants have amended the claims to reflect this distinction. Applicants therefore request the Examiner to remove the stated rejections.

In view of the amendments and remarks presented herein, Applicants believe the application is now in condition for allowance and respectfully request the Examiner to remove the stated rejections and allow all the claims.

It is believed no fee is due with this Response and Amendment. If a fee is due, please charge deposit account number 08-2442. If the Examiner has any questions, or if any information is needed to assist in expediting prosecution of the instant application, the undersigned attorney of record may be contacted at the number provided below.

Respectfully submitted,

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